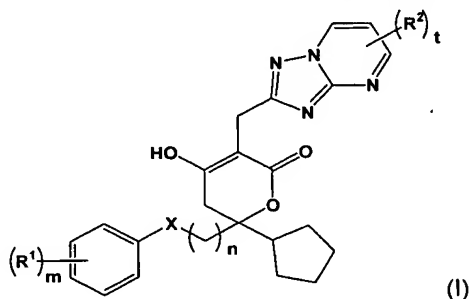


Claims

We Claim:

1. A method of increasing the bioavailability in a mammal of a first compound which is metabolized by cytochrome P450, comprising administering to said mammal said first compound and a cytochrome P450-inhibiting amount of a compound of formula (I),



wherein:

- each R^1 is independently selected from fluorine, $-C(CH_3)_2CN$, -cyclopropyl-
 10 CN, and -cyclobutyl-CN;
 each R^2 is independently selected from C_1 - C_4 alkyl, and halogen;
 X is $-CH_2-$ or $-O-$;
 m is an integer from 0 to 5;
 n is 1 or 2;
 15 t is an integer from 0 to 3; and
 pharmaceutically acceptable salts and solvates thereof.

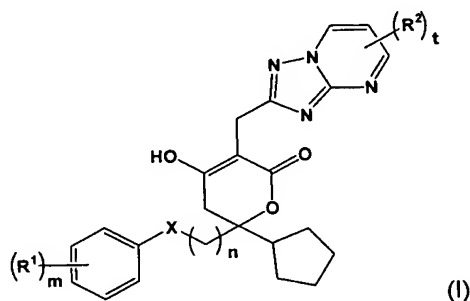
2. A method according to claim 1, wherein the cytochrome P450 is the 2D6 isoform.

3. A method according to claim 1, wherein said first compound is selected from
 20 alprenolol, amiflamine, amitriptyline, aprindine, atomoxetine, bisoprolol, brofaromine,
 bufuralol, bunitrolol, bupronolol, captopril, chlorpheniramine, chlorpromazine, cilostazol,
 cinnarizine, citalopram, clomipramine, clozapine, codeine, cyclobenzprine, debrisoquine,
 desipramine, desmethylcitalopram, dexfenfluramine, dextromethorphan, dihydrocodine,
 25 dolasetron, donezepil, doxepin, encainide, ethylmorphine, fenfluramine, flecainide, flunarizine,
 fluvoxamine, fluoxetine, fluphenazine, guanoxan, haloperidol, hydrocodone, imipramine,
 indoramin, labetalol, lidocaine, loratidine, maprotiline, (R)-methadone, meperidine,
 methamphetamine, methoxyamphetamine, 5-methoxyindoleethylamine, methoxyphenamine,
 methylenedioxymethamphetamine, metoprolol, mexiletine, mianserin, minaprine, morphine,
 30 nefazodone, nelfinavir, norcodeine, nortriptyline, ondansetron, omeprazole, oxycodone,
 paclitaxel, paroxetine, perhexiline, perphenazine, phenformin, procodine, promethazine, N-

propylajmaline, propafenone, propranolol, retinoic acid, quinidine, risperidone, ritonavir, RU-486, sparteine, tamoxifen, testosterone, thioridazine, timolol, tolterodine, tomoxatene, tramadol, trazodone, trifluoperidol, trimipramine, tropisetron, venlafaxine, vinblastine, and zuclopenthixol..

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4. A method of inhibiting cytochrome P450 activity in a mammal, comprising administering to said mammal a cytochrome P450 activity-inhibiting amount of a compound of formula (I),



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wherein:

each R^1 is independently selected from fluorine, $-C(CH_3)_2CN$, -cyclopropyl-CN, and -cyclobutyl-CN;

each R^2 is independently selected from C_1 - C_4 alkyl, and halogen;

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X is $-CH_2-$ or $-O-$;

m is an integer from 0 to 5;

n is 1 or 2;

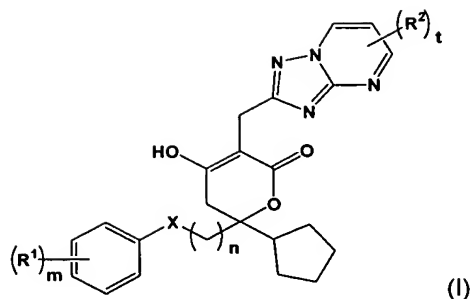
t is an integer from 0 to 3; and

pharmaceutically acceptable salts and solvates thereof.

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5. A method according to claim 4, wherein the cytochrome P450 enzyme is the 2D6 isoform.

6. A method of inhibiting cytochrome P450 enzyme activity, comprising contacting said
25 cytochrome P450 enzyme with a cytochrome P450 enzyme-inhibiting amount of a compound of formula (I),



wherein:

each R^1 is independently selected from fluorine, $-C(CH_3)_2CN$, -cyclopropyl-CN, and -cyclobutyl-CN;

each R^2 is independently selected from C_1 - C_4 alkyl, and halogen;

X is $-CH_2-$ or $-O-$;

m is an integer from 0 to 5;

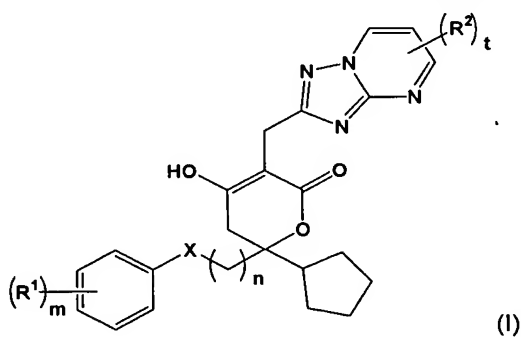
n is 1 or 2;

t is an integer from 0 to 3; and

pharmaceutically acceptable salts and solvates thereof.

7. A method according to claim 6, wherein the cytochrome P450 enzyme is the 2D6 isoform.

8. A method of decreasing the metabolism in a mammal of a first compound which is metabolized by cytochrome P450 enzyme, comprising administering to said mammal said first compound and a cytochrome P450 enzyme-inhibiting amount of a compound of formula (I),



wherein:

each R^1 is independently selected from fluorine, $-C(CH_3)_2CN$, -cyclopropyl-CN, and -cyclobutyl-CN;

each R² is independently selected from hydrogen, C₁-C₄ alkyl, and halogen;

X is -CH₂- or -O-;

m is an integer from 0 to 5;

n is 1 or 2;

t is an integer from 0 to 3; and

pharmaceutically acceptable salts and solvates thereof.

9. A method according to claim 8, wherein the cytochrome P450 enzyme is the 2D6 isoform.

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10. A method according to claim 8, wherein said first compound is selected from alprenolol, amiflamine, amitriptyline, aprindine, atomoxetine, bisoprolol, brofaromine, bufuralol, bunitrolol, bupronolol, captopril, chlorpheniramine, chlorpromazine, cilostazol, cinnarizine, citalopram, clomipramine, clozapine, codeine, cyclobenzprine, debrisoquine, desipramine, desmethylocitalopram, dexfenfluramine, dextromethorphan, dihydrocodine, dolasetron, donepezil, doxepin, encainide, ethylmorphine, fenfluramine, flecainide, flunarizine, fluvoxamine, fluoxetine, fluphenazine, guanoxan, haloperidol, hydrocodone, imipramine, indoramin, labetalol, lidocaine, loratidine, maprotiline, (R)-methadone, meperidine, methamphetamine, methoxyamphetamine, 5-methoxyindoleethylamine, methoxyphenamine, methylenedioxymethamphetamine, metoprolol, mexiletine, mianserin, minaprine, morphine, nefazodone, nelfinavir, norcodeine, nortriptyline, ondansetron, omeprazole, oxycodone, paclitaxel, paroxetine, perhexiline, perphenazine, phenformin, procodine, promethazine, N-propylajmaline, propafenone, propanolol, retinoic acid, quinidine, risperidone, ritonavir, RU-486, sparteine, tamoxifen, testosterone, thioridazine, timolol, tolterodine, tomoxatene, tramadol, trazodone, trifluoperidol, trimipramine, tropisetron, venlafaxine, vinblastine, and zuclopenthixol..

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11. A method according to claim 1, wherein in the compound of formula (I):

each R¹ is independently selected from fluorine, -C(CH₃)₂CN, -cyclopropyl-

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CN, and -cyclobutyl-CN;

each R² is independently selected from hydrogen, C₁-C₄ alkyl, and halogen;

X is -CH₂-;

m is an integer from 0 to 3;

n is 1 or 2;

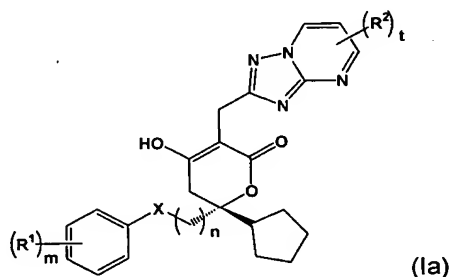
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t is an integer from 0 to 3; and

pharmaceutically acceptable salts and solvates thereof.

12. A method according to claim 11, wherein in the compound of formula (I):
 each R^1 is independently selected from fluorine, $-C(CH_3)_2CN$, -cyclopropyl-CN, and -cyclobutyl-CN;
 each R^2 is independently selected from hydrogen, C_1 - C_4 alkyl, and halogen;
 X is $-CH_2-$;
 m is 1, 2 or 3;
 n is 1;
 t is 0, 1, or 2; and
 pharmaceutically acceptable salts and solvates thereof.

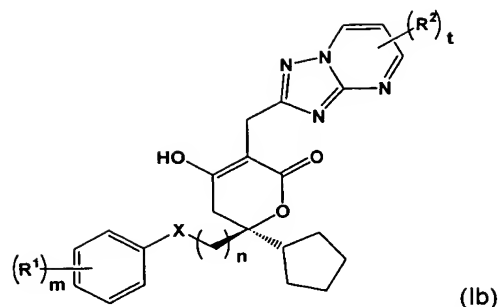
13. A method according to claim 1, wherein the compound of formula (I) is selected from those of formula (Ia):



wherein:

- each R^1 is independently selected from fluorine, $-C(CH_3)_2CN$, -cyclopropyl-CN, and -cyclobutyl-CN;
 each R^2 is independently selected from C_1 - C_4 alkyl, and halogen;
 X is $-CH_2-$ or $-O-$;
 m is an integer from 0 to 5;
 n is 1 or 2;
 t is an integer from 0 to 3; and
 pharmaceutically acceptable salts and solvates thereof.

14. A method according to claim 1, wherein the compound of formula (I) is selected from those of formula (Ib):



wherein:

each R^1 is independently selected from fluorine, $-C(CH_3)_2CN$, -cyclopropyl-CN, and -cyclobutyl-CN;

5 each R^2 is independently selected from hydrogen, C_1 - C_4 alkyl, and halogen;
X is $-CH_2-$ or $-O-$;

m is an integer from 0 to 5;

n is 1 or 2;

t is an integer from 0 to 3; and

10 pharmaceutically acceptable salts and solvates thereof.

- 15 15. A method according to claim 1, wherein the compound of formula (I) is selected from 2-[4-(2-{2-cyclopentyl-5-[(5,7-dimethyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl]-2-methylpropanenitrile; 6-cyclopentyl-3-[(5,7-dimethyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-[2-(3-ethyl-4-hydroxyphenyl)ethyl]-4-hydroxy-5,6-dihydro-2H-pyran-2-one; 1-[4-(2-{2-cyclopentyl-5-[(5,7-dimethyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl]cyclopropanecarbonitrile; 2-[4-(2-{2-cyclopentyl-4-hydroxy-5-[(6-methyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl]-2-methylpropanenitrile; 2-[4-(2-{2-cyclopentyl-5-[(5,7-dimethyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl]-2-methylpropanenitrile; 2-[4-(2-{2-cyclopentyl-5-[(5,7-dimethyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl]-2-methylpropanenitrile; 6-[2-(3-chloro-5-ethyl-4-hydroxyphenyl)ethyl]-6-cyclopentyl-3-[(5,7-dimethyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-4-hydroxy-5,6-dihydro-2H-pyran-2-one; 2-[4-(2-{2-cyclopentyl-5-[(5,7-dimethyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2,6-difluorophenyl]-2-methylpropanenitrile; 2-[4-(2-{2-cyclopentyl-4-hydroxy-5-[(6-methyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl]-2-methylpropanenitrile; 1-[4-(2-{2-cyclopentyl-4-hydroxy-5-[(6-methyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl]cyclopropanecarbonitrile; 1-(4-[2-[2-cyclopentyl-4-hydroxy-6-oxo-5-
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- ((1,2,4)triazolo[1,5-a]pyrimidin-2-ylmethyl)-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl)cyclopropanecarbonitrile; 2-[4-(2-(2-cyclopentyl-4-hydroxy-5-[(6-methyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl)ethyl)-2,6-difluorophenyl]-2-methylpropanenitrile; 1-[4-(2-(5-[(6-chloro[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-2-cyclopentyl-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl)ethyl)-2-fluorophenyl)cyclopropanecarbonitrile; 2-[4-(2-(2-cyclopentyl-4-hydroxy-5-[(4-methyl-1H-imidazol-5-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl)ethyl)-2-fluorophenyl]-2-methylpropanenitrile; 2-[4-((2-cyclopentyl-5-[(5,7-dimethyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl)methoxy)-2-fluorophenyl]-2-methylpropanenitrile; 2-[4-((2-cyclopentyl-4-hydroxy-5-[(6-methyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl)methoxy)-2-fluorophenyl]-2-methylpropanenitrile; 2-(4-(2-(2-cyclopentyl-4-hydroxy-6-oxo-5-[(1,2,4)triazolo[1,5-a]pyrimidin-2-ylmethyl)-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl)-2-methylpropanenitrile; 2-[4-(2-(5-[(6-chloro[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-2-cyclopentyl-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl)ethyl)-2-fluorophenyl]-2-methylpropanenitrile; 2-(4-(2-(2-cyclopentyl-4-hydroxy-6-oxo-5-[(1,2,4)triazolo[1,5-a]pyrimidin-2-ylmethyl)-3,6-dihydro-2H-pyran-2-yl}ethyl)-2,6-difluorophenyl)-2-methylpropanenitrile; 2-(4-(2-(2-cyclopentyl-4-hydroxy-5-(imidazo[1,2-a]pyridin-2-ylmethyl)-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl)-2-methylpropanenitrile; 3-[(6-chloro[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-cyclopentyl-6-(2-[3-fluoro-4-(1-hydroxy-1-methylethyl)phenyl]ethyl)-4-hydroxy-5,6-dihydro-2H-pyran-2-one; 1-[4-(2-(2-cyclopentyl-4-hydroxy-5-[(6-methyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl)ethyl)-2-fluorophenyl)cyclopropanecarbonitrile; 1-[4-(2-(2-cyclopentyl-4-hydroxy-5-[(6-methyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl)ethyl)-2-fluorophenyl)cyclopropanecarbonitrile; 1-(4-(2-(2-cyclopentyl-4-hydroxy-6-oxo-5-[(1,2,4)triazolo[1,5-a]pyrimidin-2-ylmethyl)-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl)cyclopropanecarbonitrile; 1-(4-(2-(2-cyclopentyl-4-hydroxy-6-oxo-5-[(1,2,4)triazolo[1,5-a]pyrimidin-2-ylmethyl)-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl)cyclopropanecarbonitrile; 1-(4-(2-(2-cyclopentyl-5-[(5,7-dimethyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl)ethyl)-2-fluorophenyl)cyclopropanecarbonitrile; 2-[4-(2-(2-cyclopentyl-5-[(6-ethyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl)ethyl)-2,6-difluorophenyl]-2-methylpropanenitrile; 1-[4-(2-(2-cyclopentyl-4-hydroxy-5-[(6-methyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl)ethyl)-2,6-difluorophenyl)cyclopropanecarbonitrile; 2-[4-(2-(2-cyclopentyl-4-hydroxy-5-[(6-methyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl)ethyl)-2,6-difluorophenyl]-2-methylpropanenitrile; 2-[4-(2-(2-cyclopentyl-4-hydroxy-5-[(6-

methyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl)ethyl)-2,6-difluorophenyl]-2-methylpropanenitrile; 2-[4-(2-{2-cyclopentyl-4-hydroxy-5-[(6-methyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl)ethyl)-2-fluoro-5-methoxyphenyl]-2-methylpropanenitrile; 2-[4-(2-{5-[(6-chloro[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-2-cyclopentyl-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl)ethyl)-2,6-difluorophenyl]-2-methylpropanenitrile; 2-[4-(2-{5-[(6-chloro[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-2-cyclopentyl-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl)ethyl)-2,6-difluorophenyl]-2-methylpropanenitrile; 2-[4-(2-{5-[(6-chloro[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-2-cyclopentyl-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl)ethyl)-2-fluorophenyl]-2-methylpropanenitrile; 2-[4-(2-{5-[(6-chloro[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-2-cyclopentyl-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl)ethyl)-2-fluorophenyl]-2-methylpropanenitrile; and pharmaceutically acceptable salts and solvates thereof.

16. A method according to claim 1, wherein the compound of formula (I) is selected from the (R)-enantiomers of 2-[4-(2-{2-cyclopentyl-5-[(5,7-dimethyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl)ethyl)-2-fluorophenyl]-2-methylpropanenitrile; 6-cyclopentyl-3-[(5,7-dimethyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-[2-(3-ethyl-4-hydroxyphenyl)ethyl]-4-hydroxy-5,6-dihydro-2H-pyran-2-one; 1-[4-(2-{2-cyclopentyl-5-[(5,7-dimethyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl)ethyl)-2-fluorophenyl]cyclopropanecarbonitrile; 2-[4-(2-{2-cyclopentyl-4-hydroxy-5-[(6-methyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl)ethyl)-2-fluorophenyl]-2-methylpropanenitrile; 2-[4-(2-{2-cyclopentyl-5-[(5,7-dimethyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl)ethyl)-2-fluorophenyl]-2-methylpropanenitrile; 2-[4-(2-{2-cyclopentyl-5-[(5,7-dimethyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl)ethyl)-2-fluorophenyl]-2-methylpropanenitrile; 6-[2-(3-chloro-5-ethyl-4-hydroxyphenyl)ethyl]-6-cyclopentyl-3-[(5,7-dimethyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-4-hydroxy-5,6-dihydro-2H-pyran-2-one; 2-[4-(2-{2-cyclopentyl-5-[(5,7-dimethyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl)ethyl)-2,6-difluorophenyl]-2-methylpropanenitrile; 2-[4-(2-{2-cyclopentyl-4-hydroxy-5-[(6-methyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl)ethyl)-2-fluorophenyl]-2-methylpropanenitrile; 1-[4-(2-{2-cyclopentyl-4-hydroxy-5-[(6-methyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl)ethyl)-2-fluorophenyl]cyclopropanecarbonitrile; 1-(4-{2-[2-cyclopentyl-4-hydroxy-6-oxo-5-[(1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-3,6-dihydro-2H-pyran-2-yl)ethyl)-2-fluorophenyl)cyclopropanecarbonitrile; 2-[4-(2-{2-cyclopentyl-4-hydroxy-5-[(6-methyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl)ethyl)-2,6-

difluorophenyl]-2-methylpropanenitrile; 1-[4-(2-{5-[(6-chloro[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-2-cyclopentyl-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl]cyclopropanecarbonitrile; 2-[4-(2-{2-cyclopentyl-4-hydroxy-5-[(4-methyl-1H-imidazol-5-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl]-2-methylpropanenitrile; 2-[4-({2-cyclopentyl-5-[(5,7-dimethyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl}methoxy)-2-fluorophenyl]-2-methylpropanenitrile; 2-[4-({2-cyclopentyl-4-hydroxy-5-[(6-methyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl}methoxy)-2-fluorophenyl]-2-methylpropanenitrile; 2-(4-{2-[2-cyclopentyl-4-hydroxy-6-oxo-5-([1,2,4]triazolo[1,5-a]pyrimidin-2-ylmethyl)-3,6-dihydro-2H-pyran-2-yl]ethyl}-2-fluorophenyl)-2-methylpropanenitrile; 2-[4-(2-{5-[(6-chloro[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-2-cyclopentyl-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl]-2-methylpropanenitrile; 2-(4-{2-[2-cyclopentyl-4-hydroxy-6-oxo-5-([1,2,4]triazolo[1,5-a]pyrimidin-2-ylmethyl)-3,6-dihydro-2H-pyran-2-yl]ethyl}-2,6-difluorophenyl)-2-methylpropanenitrile; 2-(4-{2-[2-cyclopentyl-4-hydroxy-5-(imidazo[1,2-a]pyridin-2-ylmethyl)-6-oxo-3,6-dihydro-2H-pyran-2-yl]ethyl}-2-fluorophenyl)-2-methylpropanenitrile; 3-[(6-chloro[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-cyclopentyl-6-{2-[3-fluoro-4-(1-hydroxy-1-methylethyl)phenyl]ethyl}-4-hydroxy-5,6-dihydro-2H-pyran-2-one; 1-[4-(2-{2-cyclopentyl-4-hydroxy-5-[(6-methyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl]cyclopropanecarbonitrile; 1-[4-(2-{2-cyclopentyl-4-hydroxy-5-[(6-methyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl]cyclopropanecarbonitrile; 1-(4-{2-[2-cyclopentyl-4-hydroxy-6-oxo-5-([1,2,4]triazolo[1,5-a]pyrimidin-2-ylmethyl)-3,6-dihydro-2H-pyran-2-yl]ethyl}-2-fluorophenyl)cyclopropanecarbonitrile; 1-(4-{2-[2-cyclopentyl-4-hydroxy-6-oxo-5-([1,2,4]triazolo[1,5-a]pyrimidin-2-ylmethyl)-3,6-dihydro-2H-pyran-2-yl]ethyl}-2-fluorophenyl)cyclopropanecarbonitrile; 1-[4-(2-{2-cyclopentyl-5-[(5,7-dimethyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl]cyclopropanecarbonitrile; 2-[4-(2-{2-cyclopentyl-5-[(6-ethyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2,6-difluorophenyl]-2-methylpropanenitrile; 1-[4-(2-{2-cyclopentyl-4-hydroxy-5-[(6-methyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2,6-difluorophenyl]cyclopropanecarbonitrile; 2-[4-(2-{2-cyclopentyl-4-hydroxy-5-[(6-methyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2,6-difluorophenyl]-2-methylpropanenitrile; 2-[4-(2-{2-cyclopentyl-4-hydroxy-5-[(6-methyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2,6-difluorophenyl]-2-methylpropanenitrile; 2-[4-(2-{2-cyclopentyl-4-hydroxy-5-[(6-methyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2,6-difluorophenyl]-2-methylpropanenitrile; 2-[4-(2-{2-cyclopentyl-4-hydroxy-5-[(6-methyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2,6-difluorophenyl]-2-methylpropanenitrile; 2-[4-(2-{2-cyclopentyl-4-hydroxy-5-[(6-methyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-

- fluoro-5-methoxyphenyl]-2-methylpropanenitrile; 2-[4-(2-{5-[(6-chloro[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-2-cyclopentyl-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2,6-difluorophenyl]-2-methylpropanenitrile; 2-[4-(2-{5-[(6-chloro[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-2-cyclopentyl-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2,6-difluorophenyl]-2-methylpropanenitrile; 2-[4-(2-{5-[(6-chloro[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-2-cyclopentyl-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl]-2-methylpropanenitrile; 2-[4-(2-{5-[(6-chloro[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-2-cyclopentyl-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl]-2-methylpropanenitrile; and pharmaceutically acceptable salts and solvates thereof.
17. A method according to claim 1, wherein the compound of formula (I) is selected from the (S)-enantiomers of 2-[4-(2-{2-cyclopentyl-5-[(5,7-dimethyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl]-2-methylpropanenitrile; 6-cyclopentyl-3-[(5,7-dimethyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-[2-(3-ethyl-4-hydroxyphenyl)ethyl]-4-hydroxy-5,6-dihydro-2H-pyran-2-one; 1-[4-(2-{2-cyclopentyl-5-[(5,7-dimethyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl]cyclopropanecarbonitrile; 2-[4-(2-{2-cyclopentyl-4-hydroxy-5-[(6-methyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl]-2-methylpropanenitrile; 2-[4-(2-{2-cyclopentyl-5-[(5,7-dimethyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl]-2-methylpropanenitrile; 2-[4-(2-{2-cyclopentyl-5-[(5,7-dimethyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl]-2-methylpropanenitrile; 6-[2-(3-chloro-5-ethyl-4-hydroxyphenyl)ethyl]-6-cyclopentyl-3-[(5,7-dimethyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-4-hydroxy-5,6-dihydro-2H-pyran-2-one; 2-[4-(2-{2-cyclopentyl-5-[(5,7-dimethyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2,6-difluorophenyl]-2-methylpropanenitrile; 2-[4-(2-{2-cyclopentyl-4-hydroxy-5-[(6-methyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl]-2-methylpropanenitrile; 1-[4-(2-{2-cyclopentyl-4-hydroxy-5-[(6-methyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl]cyclopropanecarbonitrile; 1-(4-{2-[2-cyclopentyl-4-hydroxy-6-oxo-5-[(1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl]cyclopropanecarbonitrile; 2-[4-(2-{2-cyclopentyl-4-hydroxy-5-[(6-methyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2,6-difluorophenyl]-2-methylpropanenitrile; 1-[4-(2-{5-[(6-chloro[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-2-cyclopentyl-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl]cyclopropanecarbonitrile; 2-[4-(2-{2-cyclopentyl-4-hydroxy-5-[(4-methyl-1H-

- imidazol-5-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl)ethyl)-2-fluorophenyl]-2-methylpropanenitrile; 2-[4-({2-cyclopentyl-5-[(5,7-dimethyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl)methoxy)-2-fluorophenyl]-2-methylpropanenitrile; 2-[4-({2-cyclopentyl-4-hydroxy-5-[(6-methyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl)methoxy)-2-fluorophenyl]-2-methylpropanenitrile; 2-(4-{2-[2-cyclopentyl-4-hydroxy-6-oxo-5-[(1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl)-2-methylpropanenitrile; 2-[4-(2-{5-[(6-chloro[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-2-cyclopentyl-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl]-2-methylpropanenitrile; 2-(4-{2-[2-cyclopentyl-4-hydroxy-6-oxo-5-[(1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-3,6-dihydro-2H-pyran-2-yl}ethyl)-2,6-difluorophenyl)-2-methylpropanenitrile; 2-(4-{2-[2-cyclopentyl-4-hydroxy-5-(imidazo[1,2-a]pyridin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl)-2-methylpropanenitrile; 3-[(6-chloro[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-cyclopentyl-6-(2-[3-fluoro-4-(1-hydroxy-1-methylethyl)phenyl]ethyl)-4-hydroxy-5,6-dihydro-2H-pyran-2-one; 1-[4-(2-{2-cyclopentyl-4-hydroxy-5-[(6-methyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl]cyclopropanecarbonitrile; 1-[4-(2-{2-cyclopentyl-4-hydroxy-5-[(6-methyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl]cyclopropanecarbonitrile; 1-(4-{2-[2-cyclopentyl-4-hydroxy-6-oxo-5-[(1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl)cyclopropanecarbonitrile; 1-(4-{2-[2-cyclopentyl-4-hydroxy-6-oxo-5-[(1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl)cyclopropanecarbonitrile; 1-[4-(2-{2-cyclopentyl-5-[(5,7-dimethyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl]cyclopropanecarbonitrile; 2-[4-(2-{2-cyclopentyl-5-[(6-ethyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2,6-difluorophenyl]-2-methylpropanenitrile; 1-[4-(2-{2-cyclopentyl-4-hydroxy-5-[(6-methyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2,6-difluorophenyl]cyclopropanecarbonitrile; 2-[4-(2-{2-cyclopentyl-4-hydroxy-5-[(6-methyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2,6-difluorophenyl]-2-methylpropanenitrile; 2-[4-(2-{2-cyclopentyl-4-hydroxy-5-[(6-methyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2,6-difluorophenyl]-2-methylpropanenitrile; 2-[4-(2-{2-cyclopentyl-4-hydroxy-5-[(6-methyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluoro-5-methoxyphenyl]-2-methylpropanenitrile; 2-[4-(2-{5-[(6-chloro[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-2-cyclopentyl-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2,6-difluorophenyl]-2-methylpropanenitrile; 2-[4-(2-{5-[(6-chloro[1,2,4]triazolo[1,5-a]pyrimidin-2-

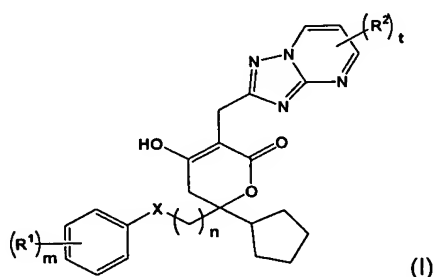
yl)methyl]-2-cyclopentyl-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl)ethyl)-2,6-difluorophenyl]-
 2-methylpropanenitrile; 2-[4-(2-{5-[(6-chloro[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-2-
 cyclopentyl-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl)ethyl)-2-fluorophenyl]-2-
 methylpropanenitrile; 2-[4-(2-{5-[(6-chloro[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-2-
 5 cyclopentyl-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl)ethyl)-2-fluorophenyl]-2-
 methylpropanenitrile; and pharmaceutically acceptable salts and solvates thereof.

18. A method according to claim 1, wherein the compound of formula (I) is substantially
 enantiomerically pure.

10

19. A method according to claim 1, wherein the compound of formula (I) is
 enantiomerically pure.

20. A composition, comprising a first compound that is metabolized by at least one
 15 cytochrome P450 enzyme and a cytochrome P450 enzyme activity-inhibiting amount of a
 compound of formula (I),



wherein:

20 each R^1 is independently selected from fluorine, $-C(CH_3)_2CN$, -cyclopropyl-
 CN, and -cyclobutyl-CN;
 each R^2 is independently selected from hydrogen, C_1 - C_4 alkyl, and halogen;
 X is $-CH_2-$ or $-O-$;
 m is an integer from 0 to 5;
 25 n is 1 or 2;
 t is an integer from 0 to 3; and
 pharmaceutically acceptable salts and solvates thereof.

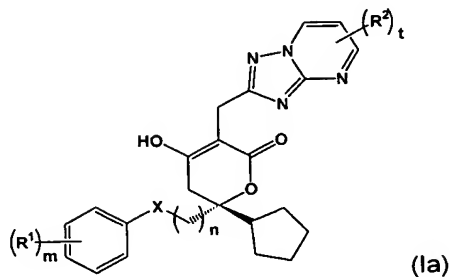
21. A composition according to claim 20, wherein said at least one cytochrome P450
 30 enzyme is the 2D6 isoform.

22. A composition according to claim 20, wherein said first compound is selected from alprenolol, amiflamine, amitriptyline, aprindine, atomoxetine, bisoprolol, brofaromine, bufuralol, bunitrolol, bupronolol, captopril, chlorpheniramine, chlorpromazine, cilostazol, cinnarizine, citalopram, clomipramine, clozapine, codeine, cyclobenzprine, debrisoquine, desipramine, desmethylocitalopram, dexfenfluramine, dextromethorphan, dihydrocodine, dolasetron, donezepil, doxepin, encainide, ethylmorphine, fenfluramine, flecainide, flunarizine, fluvoxamine, fluoxetine, fluphenazine, guanoxan, haloperidol, hydrocodone, imipramine, indoramin, labetalol, lidocaine, loratidine, maprotiline, (R)-methadone, meperidine, methamphetamine, methoxyamphetamine, 5-methoxyindoleethylamine, methoxyphenamine, methylenedioxymethamphetamine, metoprolol, mexiletine, mianserin, minaprine, morphine, nefazodone, nelfinavir, norcodeine, nortriptyline, ondansetron, omeprazole, oxycodone, paclitaxel, paroxetine, perhexiline, perphenazine, phenformin, procodine, promethazine, N-propylajmaline, propafenone, propanolol, retinoic acid, quinidine, risperidone, ritonavir, RU-486, sparteine, tamoxifen, testosterone, thioridazine, timolol, tolterodine, tomoxatene, tramadol, trazodone, trifluoperidol, trimipramine, tropisetron, venlafaxine, vinblastine, and zuclopenthixol..

23. A composition according to claim 20, wherein in the compound of formula (I):
each R¹ is independently selected from fluorine, -C(CH₃)₂CN, -cyclopropyl-CN, and -cyclobutyl-CN;
each R² is independently selected from hydrogen, C₁-C₄ alkyl, and halogen;
X is -CH₂-;
m is an integer from 0 to 3;
n is 1 or 2;
t is an integer from 0 to 3; and
pharmaceutically acceptable salts and solvates thereof.

24. A composition according to claim 20, wherein in the compound of formula (I):
each R¹ is independently selected from fluorine, -C(CH₃)₂CN, -cyclopropyl-CN, and -cyclobutyl-CN;
each R² is independently selected from hydrogen, C₁-C₄ alkyl, and halogen;
X is -CH₂-;
m is 1, 2 or 3;
n is 1;
t is 0, 1, or 2; and
pharmaceutically acceptable salts and solvates thereof.

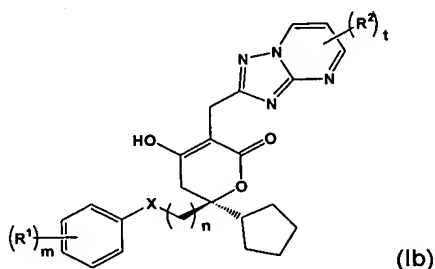
25. A composition according to claim 20, wherein the compound of formula (I) is selected from those of formula (Ia):



wherein:

- 5 each R^1 is independently selected from fluorine, $-C(CH_3)_2CN$, -cyclopropyl-CN, and -cyclobutyl-CN;
 each R^2 is independently selected from hydrogen, C_1 - C_4 alkyl, and halogen;
 X is $-CH_2-$ or $-O-$;
 m is an integer from 0 to 5;
 10 n is 1 or 2;
 t is an integer from 0 to 3; and
 pharmaceutically acceptable salts and solvates thereof.

26. A composition according to claim 20, wherein the compound of formula (I) is selected from those of formula (Ib):



wherein:

- 20 each R^1 is independently selected from fluorine, $-C(CH_3)_2CN$, -cyclopropyl-CN, and -cyclobutyl-CN;
 each R^2 is independently selected from hydrogen, C_1 - C_4 alkyl, and halogen;
 X is $-CH_2-$ or $-O-$;
 m is an integer from 0 to 5;
 n is 1 or 2;
 t is an integer from 0 to 3; and
 25 pharmaceutically acceptable salts and solvates thereof.

27. A composition according to claim 20, wherein the compound of formula (I) is selected from 2-[4-(2-{2-cyclopentyl-5-[(5,7-dimethyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl]-2-methylpropanenitrile; 6-cyclopentyl-3-[(5,7-dimethyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-[2-(3-ethyl-4-hydroxyphenyl)ethyl]-4-hydroxy-5,6-dihydro-2H-pyran-2-one; 1-[4-(2-{2-cyclopentyl-5-[(5,7-dimethyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl]cyclopropanecarbonitrile; 2-[4-(2-{2-cyclopentyl-4-hydroxy-5-[(6-methyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl]-2-methylpropanenitrile; 2-[4-(2-{2-cyclopentyl-5-[(5,7-dimethyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl]-2-methylpropanenitrile; 2-[4-(2-{2-cyclopentyl-5-[(5,7-dimethyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl]-2-methylpropanenitrile; 6-[2-(3-chloro-5-ethyl-4-hydroxyphenyl)ethyl]-6-cyclopentyl-3-[(5,7-dimethyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-4-hydroxy-5,6-dihydro-2H-pyran-2-one; 2-[4-(2-{2-cyclopentyl-5-[(5,7-dimethyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2,6-difluorophenyl]-2-methylpropanenitrile; 2-[4-(2-{2-cyclopentyl-4-hydroxy-5-[(6-methyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl]-2-methylpropanenitrile; 1-[4-(2-{2-cyclopentyl-4-hydroxy-5-[(6-methyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl]cyclopropanecarbonitrile; 1-(4-{2-[2-cyclopentyl-4-hydroxy-6-oxo-5-[(1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl)cyclopropanecarbonitrile; 2-[4-(2-{2-cyclopentyl-4-hydroxy-5-[(6-methyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2,6-difluorophenyl]-2-methylpropanenitrile; 1-[4-(2-{5-[(6-chloro[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-2-cyclopentyl-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl]cyclopropanecarbonitrile; 2-[4-(2-{2-cyclopentyl-4-hydroxy-5-[(4-methyl-1H-imidazol-5-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl]-2-methylpropanenitrile; 2-[4-(2-{2-cyclopentyl-5-[(5,7-dimethyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl}methoxy)-2-fluorophenyl]-2-methylpropanenitrile; 2-[4-(2-{2-cyclopentyl-4-hydroxy-5-[(6-methyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl}methoxy)-2-fluorophenyl]-2-methylpropanenitrile; 2-(4-{2-[2-cyclopentyl-4-hydroxy-6-oxo-5-[(1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl)-2-methylpropanenitrile; 2-[4-(2-{5-[(6-chloro[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-2-cyclopentyl-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl]-2-methylpropanenitrile; 2-(4-{2-[2-cyclopentyl-4-hydroxy-6-oxo-5-[(1,2,4]triazolo[1,5-

- a]pyrimidin-2-ylmethyl)-3,6-dihydro-2H-pyran-2-yl]ethyl)-2,6-difluorophenyl)-2-methylpropanenitrile; 2-(4-{2-[2-cyclopentyl-4-hydroxy-5-(imidazo[1,2-a]pyridin-2-ylmethyl)-6-oxo-3,6-dihydro-2H-pyran-2-yl]ethyl)-2-fluorophenyl)-2-methylpropanenitrile; 3-[(6-chloro[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-cyclopentyl-6-{2-[3-fluoro-4-(1-hydroxy-1-methylethyl)phenyl]ethyl)-4-hydroxy-5,6-dihydro-2H-pyran-2-one; 1-[4-(2-{2-cyclopentyl-4-hydroxy-5-[(6-methyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl]ethyl)-2-fluorophenyl]cyclopropanecarbonitrile; 1-[4-(2-{2-cyclopentyl-4-hydroxy-5-[(6-methyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl]ethyl)-2-fluorophenyl]cyclopropanecarbonitrile; 1-(4-{2-[2-cyclopentyl-4-hydroxy-6-oxo-5-([1,2,4]triazolo[1,5-a]pyrimidin-2-ylmethyl)-3,6-dihydro-2H-pyran-2-yl]ethyl)-2-fluorophenyl)cyclopropanecarbonitrile; 1-(4-{2-[2-cyclopentyl-4-hydroxy-6-oxo-5-([1,2,4]triazolo[1,5-a]pyrimidin-2-ylmethyl)-3,6-dihydro-2H-pyran-2-yl]ethyl)-2-fluorophenyl)cyclopropanecarbonitrile; 1-[4-(2-{2-cyclopentyl-5-[(5,7-dimethyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl]ethyl)-2-fluorophenyl]cyclopropanecarbonitrile; 2-[4-(2-{2-cyclopentyl-5-[(6-ethyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl]ethyl)-2,6-difluorophenyl)-2-methylpropanenitrile; 1-[4-(2-{2-cyclopentyl-4-hydroxy-5-[(6-methyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl]ethyl)-2,6-difluorophenyl]cyclopropanecarbonitrile; 2-[4-(2-{2-cyclopentyl-4-hydroxy-5-[(6-methyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl]ethyl)-2,6-difluorophenyl)-2-methylpropanenitrile; 2-[4-(2-{2-cyclopentyl-4-hydroxy-5-[(6-methyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl]ethyl)-2,6-difluorophenyl)-2-methylpropanenitrile; 2-[4-(2-{2-cyclopentyl-4-hydroxy-5-[(6-methyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl]ethyl)-2-fluoro-5-methoxyphenyl)-2-methylpropanenitrile; 2-[4-(2-{5-[(6-chloro[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-2-cyclopentyl-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl]ethyl)-2,6-difluorophenyl)-2-methylpropanenitrile; 2-[4-(2-{5-[(6-chloro[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-2-cyclopentyl-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl]ethyl)-2,6-difluorophenyl)-2-methylpropanenitrile; 2-[4-(2-{5-[(6-chloro[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-2-cyclopentyl-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl]ethyl)-2-fluorophenyl)-2-methylpropanenitrile; 2-[4-(2-{5-[(6-chloro[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-2-cyclopentyl-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl]ethyl)-2-fluorophenyl)-2-methylpropanenitrile; and pharmaceutically acceptable salts and solvates thereof.
28. A composition according to claim 20, wherein the compound of formula (I) is selected from the (R)-enantiomers of 2-[4-(2-{2-cyclopentyl-5-[(5,7-dimethyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl]ethyl)-2-fluorophenyl)-2-

methylpropanenitrile; 6-cyclopentyl-3-[(5,7-dimethyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-[2-(3-ethyl-4-hydroxyphenyl)ethyl]-4-hydroxy-5,6-dihydro-2H-pyran-2-one; 1-[4-(2-{2-cyclopentyl-5-[(5,7-dimethyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl]cyclopropanecarbonitrile; 2-[4-(2-{2-cyclopentyl-4-hydroxy-5-[(6-methyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl]-2-methylpropanenitrile; 2-[4-(2-{2-cyclopentyl-5-[(5,7-dimethyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl]-2-methylpropanenitrile; 2-[4-(2-{2-cyclopentyl-5-[(5,7-dimethyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl]-2-methylpropanenitrile; 6-[2-(3-chloro-5-ethyl-4-hydroxyphenyl)ethyl]-6-cyclopentyl-3-[(5,7-dimethyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-4-hydroxy-5,6-dihydro-2H-pyran-2-one; 2-[4-(2-{2-cyclopentyl-5-[(5,7-dimethyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2,6-difluorophenyl]-2-methylpropanenitrile; 2-[4-(2-{2-cyclopentyl-4-hydroxy-5-[(6-methyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl]-2-methylpropanenitrile; 1-[4-(2-{2-cyclopentyl-4-hydroxy-5-[(6-methyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl]cyclopropanecarbonitrile; 1-(4-{2-[2-cyclopentyl-4-hydroxy-6-oxo-5-[(1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl)cyclopropanecarbonitrile; 2-[4-(2-{2-cyclopentyl-4-hydroxy-5-[(6-methyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2,6-difluorophenyl]-2-methylpropanenitrile; 1-[4-(2-{5-[(6-chloro[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-2-cyclopentyl-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl]cyclopropanecarbonitrile; 2-[4-(2-{2-cyclopentyl-4-hydroxy-5-[(4-methyl-1H-imidazol-5-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl]-2-methylpropanenitrile; 2-[4-(2-{2-cyclopentyl-5-[(5,7-dimethyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl}methoxy)-2-fluorophenyl]-2-methylpropanenitrile; 2-[4-(2-{2-cyclopentyl-4-hydroxy-5-[(6-methyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl}methoxy)-2-fluorophenyl]-2-methylpropanenitrile; 2-(4-{2-[2-cyclopentyl-4-hydroxy-6-oxo-5-[(1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl)-2-methylpropanenitrile; 2-[4-(2-{5-[(6-chloro[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-2-cyclopentyl-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl]-2-methylpropanenitrile; 2-(4-{2-[2-cyclopentyl-4-hydroxy-6-oxo-5-[(1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-3,6-dihydro-2H-pyran-2-yl}ethyl)-2,6-difluorophenyl)-2-methylpropanenitrile; 2-(4-{2-[2-cyclopentyl-4-hydroxy-5-(imidazo[1,2-a]pyridin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl)-2-methylpropanenitrile; 3-[(6-

chloro[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-cyclopentyl-6-{2-[3-fluoro-4-(1-hydroxy-1-methylethyl)phenyl]ethyl}-4-hydroxy-5,6-dihydro-2H-pyran-2-one; 1-[4-(2-{2-cyclopentyl-4-hydroxy-5-[(6-methyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl]cyclopropanecarbonitrile; 1-[4-(2-{2-cyclopentyl-4-hydroxy-5-[(6-methyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl]cyclopropanecarbonitrile; 1-(4-{2-[2-cyclopentyl-4-hydroxy-6-oxo-5-[(1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl)cyclopropanecarbonitrile; 1-(4-{2-[2-cyclopentyl-4-hydroxy-6-oxo-5-[(1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl)cyclopropanecarbonitrile; 1-[4-(2-{2-cyclopentyl-5-[(5,7-dimethyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl]cyclopropanecarbonitrile; 2-[4-(2-{2-cyclopentyl-5-[(6-ethyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2,6-difluorophenyl]-2-methylpropanenitrile; 1-[4-(2-{2-cyclopentyl-4-hydroxy-5-[(6-methyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2,6-difluorophenyl]cyclopropanecarbonitrile; 2-[4-(2-{2-cyclopentyl-4-hydroxy-5-[(6-methyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2,6-difluorophenyl]-2-methylpropanenitrile; 2-[4-(2-{2-cyclopentyl-4-hydroxy-5-[(6-methyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2,6-difluorophenyl]-2-methylpropanenitrile; 2-[4-(2-{2-cyclopentyl-4-hydroxy-5-[(6-fluoro-5-methoxyphenyl)-2-methylpropanenitrile; 2-[4-(2-{5-[(6-chloro[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-2-cyclopentyl-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2,6-difluorophenyl]-2-methylpropanenitrile; 2-[4-(2-{5-[(6-chloro[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-2-cyclopentyl-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2,6-difluorophenyl]-2-methylpropanenitrile; 2-[4-(2-{5-[(6-chloro[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-2-cyclopentyl-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl]-2-methylpropanenitrile; 2-[4-(2-{5-[(6-chloro[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-2-cyclopentyl-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl]-2-methylpropanenitrile; and pharmaceutically acceptable salts and solvates thereof.

29. A composition according to claim 20, wherein the compound of formula (I) is selected from the (S)-enantiomers of 2-[4-(2-{2-cyclopentyl-5-[(5,7-dimethyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl]-2-methylpropanenitrile; 6-cyclopentyl-3-[(5,7-dimethyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-[2-(3-ethyl-4-hydroxyphenyl)ethyl]-4-hydroxy-5,6-dihydro-2H-pyran-2-one; 1-[4-(2-{2-cyclopentyl-5-[(5,7-dimethyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-4-hydroxy-6-oxo-

- 3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl]cyclopropanecarbonitrile; 2-[4-(2-{2-cyclopentyl-4-hydroxy-5-[(6-methyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl]-2-methylpropanenitrile; 2-[4-(2-{2-cyclopentyl-5-[(5,7-dimethyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl]-2-methylpropanenitrile; 2-[4-(2-{2-cyclopentyl-5-[(5,7-dimethyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl]-2-methylpropanenitrile; 6-[2-(3-chloro-5-ethyl-4-hydroxyphenyl)ethyl]-6-cyclopentyl-3-[(5,7-dimethyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-4-hydroxy-5,6-dihydro-2H-pyran-2-one; 2-[4-(2-{2-cyclopentyl-5-[(5,7-dimethyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2,6-difluorophenyl]-2-methylpropanenitrile; 2-[4-(2-{2-cyclopentyl-4-hydroxy-5-[(6-methyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl]-2-methylpropanenitrile; 1-[4-(2-{2-cyclopentyl-4-hydroxy-5-[(6-methyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl]cyclopropanecarbonitrile; 1-(4-{2-[2-cyclopentyl-4-hydroxy-6-oxo-5-[(1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl]cyclopropanecarbonitrile; 2-[4-(2-{2-cyclopentyl-4-hydroxy-5-[(6-methyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2,6-difluorophenyl]-2-methylpropanenitrile; 1-[4-(2-{5-[(6-chloro[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-2-cyclopentyl-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl]cyclopropanecarbonitrile; 2-[4-(2-{2-cyclopentyl-4-hydroxy-5-[(4-methyl-1H-imidazol-5-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl]-2-methylpropanenitrile; 2-[4-((2-cyclopentyl-5-[(5,7-dimethyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl)methoxy)-2-fluorophenyl]-2-methylpropanenitrile; 2-[4-((2-cyclopentyl-4-hydroxy-5-[(6-methyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl)methoxy)-2-fluorophenyl]-2-methylpropanenitrile; 2-(4-{2-[2-cyclopentyl-4-hydroxy-6-oxo-5-[(1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl)-2-methylpropanenitrile; 2-[4-(2-{5-[(6-chloro[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-2-cyclopentyl-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl]-2-methylpropanenitrile; 2-(4-{2-[2-cyclopentyl-4-hydroxy-6-oxo-5-[(1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-3,6-dihydro-2H-pyran-2-yl}ethyl)-2,6-difluorophenyl)-2-methylpropanenitrile; 2-(4-{2-[2-cyclopentyl-4-hydroxy-5-(imidazo[1,2-a]pyridin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl)-2-methylpropanenitrile; 3-[(6-chloro[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-cyclopentyl-6-[2-[3-fluoro-4-(1-hydroxy-1-methylethyl)phenyl]ethyl]-4-hydroxy-5,6-dihydro-2H-pyran-2-one; 1-[4-(2-{2-cyclopentyl-4-hydroxy-5-[(6-methyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-

yl}ethyl)-2-fluorophenyl]cyclopropanecarbonitrile; 1-[4-(2-{2-cyclopentyl-4-hydroxy-5-[(6-methyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl]cyclopropanecarbonitrile; 1-(4-{2-[2-cyclopentyl-4-hydroxy-6-oxo-5-([1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl)cyclopropanecarbonitrile; 1-(4-{2-[2-cyclopentyl-4-hydroxy-6-oxo-5-([1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl)cyclopropanecarbonitrile; 1-[4-(2-{2-cyclopentyl-5-[(5,7-dimethyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl]cyclopropanecarbonitrile; 2-[4-(2-{2-cyclopentyl-5-[(6-ethyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2,6-difluorophenyl]-2-methylpropanenitrile; 1-[4-(2-{2-cyclopentyl-4-hydroxy-5-[(6-methyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2,6-difluorophenyl]cyclopropanecarbonitrile; 2-[4-(2-{2-cyclopentyl-4-hydroxy-5-[(6-methyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2,6-difluorophenyl]-2-methylpropanenitrile; 2-[4-(2-{2-cyclopentyl-4-hydroxy-5-[(6-methyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2,6-difluorophenyl]-2-methylpropanenitrile; 2-[4-(2-{2-cyclopentyl-4-hydroxy-5-[(6-methyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluoro-5-methoxyphenyl]-2-methylpropanenitrile; 2-[4-(2-{5-[(6-chloro[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-2-cyclopentyl-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2,6-difluorophenyl]-2-methylpropanenitrile; 2-[4-(2-{5-[(6-chloro[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-2-cyclopentyl-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2,6-difluorophenyl]-2-methylpropanenitrile; 2-[4-(2-{5-[(6-chloro[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-2-cyclopentyl-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl]-2-methylpropanenitrile; 2-[4-(2-{5-[(6-chloro[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-2-cyclopentyl-4-hydroxy-6-oxo-3,6-dihydro-2H-pyran-2-yl}ethyl)-2-fluorophenyl]-2-methylpropanenitrile; and pharmaceutically acceptable salts and solvates thereof.

30. A composition according to claim 20, wherein the compound of formula (I) is substantially enantiomerically pure.

31. A composition according to claim 20, wherein the compound of formula (I) is enantiomerically pure.

32. A method according to claim 1, wherein said first compound is chosen from antagonists of the N-methyl-D-aspartate receptor.

33. A method according to claim 32, wherein said antagonist of the N-methyl-D-aspartate receptor is (1S, 2S)-1-(4-hydroxyphenyl)-2-(4-hydroxy-4-phenylpiperidin-1-yl)-1-propanol, or a pharmaceutically acceptable salt or solvate thereof.
- 5 34. A method according to claim 8, wherein said first compound is chosen from antagonists of the N-methyl-D-aspartate receptor.
35. A method according to claim 34, wherein said antagonist of the N-methyl-D-aspartate receptor is (1S, 2S)-1-(4-hydroxyphenyl)-2-(4-hydroxy-4-phenylpiperidin-1-yl)-1-propanol, or a
10 pharmaceutically acceptable salt or solvate thereof.
36. A composition according to claim 20, wherein said first compound is chosen from antagonists of the N-methyl-D-aspartate receptor.
- 15 37. A composition according to claim 36, wherein said antagonist of the N-methyl-D-aspartate receptor is (1S, 2S)-1-(4-hydroxyphenyl)-2-(4-hydroxy-4-phenylpiperidin-1-yl)-1-propanol, or a pharmaceutically acceptable salt or solvate thereof.